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FEE TRANSMITTAL
For FY 2009

☐ Applicant claims small entity status. See 37 CFR 1.27

TOTAL AMOUNT OF PAYMENT	($)	540.00

Complete if Known	
Application Number	10/662,678
Filing Date	September 15, 2003
First Named Inventor	TROUP, John P.
Examiner Name	HA, Julie
Art Unit	1654
Attorney Docket No.	8493-US

METHOD OF PAYMENT (check all that apply)

☐ Check ☐ Credit Card ☐ Money Order ☐ None ☐ Other (please identify): _____

☑ Deposit Account Deposit Account Number: 50-4498 Deposit Account Name: Nestle Nutrition

For the above-identified deposit account, the Director is hereby authorized to: (check all that apply)

☑ Charge fee(s) indicated below ☐ Charge fee(s) indicated below, **except for the filing fee**

☑ Charge any additional fee(s) or underpayments of fee(s) under 37 CFR 1.16 and 1.17 ☑ Credit any overpayments

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FEE CALCULATION

1. BASIC FILING, SEARCH, AND EXAMINATION FEES

Application Type	FILING FEES Fee ($)	FILING FEES Small Entity Fee ($)	SEARCH FEES Fee ($)	SEARCH FEES Small Entity Fee ($)	EXAMINATION FEES Fee ($)	EXAMINATION FEES Small Entity Fee ($)	Fees Paid ($)
Utility	330	165	540	270	220	110	
Design	220	110	100	50	140	70	
Plant	220	110	330	165	170	85	
Reissue	330	165	540	270	650	325	
Provisional	220	110	0	0	0	0	

2. EXCESS CLAIM FEES

Fee Description	Fee ($)	Small Entity Fee ($)
Each claim over 20 (including Reissues)	52	26
Each independent claim over 3 (including Reissues)	220	110
Multiple dependent claims	390	195

Total Claims	Extra Claims	Fee ($)	Fee Paid ($)
_____ - 20 or HP =	_____ x	_____ =	_____

HP = highest number of total claims paid for, if greater than 20.

Indep. Claims	Extra Claims	Fee ($)	Fee Paid ($)
_____ - 3 or HP =	_____ x	_____ =	_____

HP = highest number of independent claims paid for, if greater than 3.

Multiple Dependent Claims Fee ($)	Multiple Dependent Claims Fee Paid ($)
_____	_____

3. APPLICATION SIZE FEE

If the specification and drawings exceed 100 sheets of paper (excluding electronically filed sequence or computer listings under 37 CFR 1.52(e)), the application size fee due is $270 ($135 for small entity) for each additional 50 sheets or fraction thereof. See 35 U.S.C. 41(a)(1)(G) and 37 CFR 1.16(s).

Total Sheets	Extra Sheets	Number of each additional 50 or fraction thereof	Fee ($)	Fee Paid ($)
_____ - 100 =	_____ / 50 =	_____ (round up to a whole number)	x _____	= _____

4. OTHER FEE(S)

	Fees Paid ($)
Non-English Specification, $130 fee (no small entity discount)	
Other (e.g., late filing surcharge): Filing a brief in support of an appeal under 41.20(b)(2)	540.00

SUBMITTED BY

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Name (Print/Type)	Gary M. Lobel		Date April 9, 2009

THE UNITED STATES PATENT AND TRADEMARK OFFICE
BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

In re application of: TROUP, John P. et al.	Confirmation No.: 1877
Application No.: 10/662,678	Group Art Unit: 1654
Filing Date: September 15, 2003	Examiner: HA, Julie
For: NUTRITIONAL COMPOSITIONS	Attorney Docket No.: 8493-US

MAIL STOP APPEAL BRIEF - PATENTS
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

APPELLANT'S APPEAL BRIEF

Sir:

Appellant submits this Appeal Brief in support of the Notice of Appeal filed on March 13, 2009. This Appeal is taken from the Final Rejection in the Office Action dated December 15, 2008.

I. REAL PARTY IN INTEREST

The real party in interest for the above-identified patent application on Appeal is Nestec S.A., by virtue of an Assignment recorded on February 28, 2008 at reel 020571, frames 0616-0621 in the United States Patent and Trademark Office.

II. RELATED APPEALS AND INTERFERENCES

Appellant's legal representative and the Assignees of the this patent application do not know of any prior or pending appeals, interferences or judicial proceedings that may be related to, directly affect or be directly affected by or have a bearing on the Board's decision with respect to the above-identified Appeal.

III. STATUS OF CLAIMS

Claims 1-4, 7-11, 13-14, 16-17 and 23-28 are pending in this application. Claims 6, 12 and 18-22 were previously withdrawn. Claims 5, 15 and 29 were previously canceled. Claims 1-4, 6-14 and 16-28 stand rejected. Therefore, Claims 1-4, 7-11, 13-14, 16-17 and 23-28 are being appealed in this Brief. A copy of the appealed claims is included in the Claims Appendix.

IV. STATUS OF AMENDMENTS

A final Office Action was mailed on December 15, 2008 rejecting the claims under 35 U.S.C. §112, second paragraph, and as obvious in view of several cited references. Appellant responded to the final Office Action on February 6, 2009 amending the claims to overcome the rejection under 35 U.S.C. §112, second paragraph, and obvious rejections set forth in the final Office Action. An Advisory Action withdrawing the rejection under 35 U.S.C. §112, second paragraph, and maintaining the obviousness rejections was mailed on February 24, 2009. Appellant filed a Notice of Appeal on March 13, 2009. A copy of the final Office Action and Advisory Action are attached as Exhibits A and B, respectively, in the Evidence Appendix.

V. SUMMARY OF CLAIMED SUBJECT MATTER

A summary of the claimed subject matter by way of reference to the specification and/or figures for each of the independent claims is provided as follows:

Independent Claim 1 is directed to a composition comprising: leucine (page 3, lines 7-15 and 24-27) and at least one essential amino acid selected from the group consisting of isoleucine, lysine, methionine, phenylalanine, threonine, tryptophan, valine or histidine in free and/or salt form (page 3, lines 17-22 and 29-33), wherein said leucine, in free and/or salt form, is present in an amount of at least about 25% to about 95% by weight based on the weight of total amino acids (page 3, lines 7-15 and 24-27) and wherein said composition provides a ratio of total essential amino acids to total amino acids ranging from about 0.60 to about 0.90 (page 6, lines 20-27).

Independent Claim 2 is directed to a composition comprising: leucine (page 3, lines 7-15 and 24-27) and at least one essential amino acid selected from the group consisting of isoleucine, lysine, methionine, phenylalanine, threonine, tryptophan, valine, or histidine in free and/or salt form (page 3, lines 17-22 and 29-33), wherein total leucine is present in an amount of at least about 25% to about 35% by weight based on the weight of total amino acids (page 3, lines 7-15 and 24-27) and wherein said composition provides a ratio of total essential amino acids to total amino acids ranging from about 0.60 to about 0.90 (page 6, lines 20-27).

Independent Claim 3 is directed to a composition comprising: a) leucine (page 3, lines 7-15 and 24-27) and at least one essential amino acid in free form and/or salt form selected from the group consisting of isoleucine, lysine, methionine, phenylalanine, threonine, tryptophan, valine, or histidine (page 3, lines 17-22 and 29-33) and, optionally, at least one conditionally essential amino acid selected from the group consisting of tyrosine, cysteine, arginine and glutamine in free form and/or salt form (page 3, lines 17-22 and 29-33), and b) at least one intact protein selected from the group consisting of casein, whey protein, soy protein, collagen or wheat protein (page 3, lines 1-5), wherein said composition provides a ratio of total essential amino acids and, optionally, conditionally essential amino acids to total amino acids ranging from about 0.60 to about 0.90 (page 6, lines 20-27) and wherein said leucine, in free and/or salt form, is present in an amount of at least about 25% by weight based on the weight of intact protein (page 4, lines 1-15).

Independent Claim 17 is directed to a kit (page 15, line 21-27) comprising: a) a first composition comprising: 1) leucine (page 3, lines 7-15 and 24-27) and at least one essential amino acid in free form and/or salt form selected from the group consisting of isoleucine, lysine, methionine, phenylalanine, threonine, tryptophan, valine, or histidine (page 3, lines 17-22 and 29-33) and, optionally, at least one conditionally essential amino acid selected from the group consisting of tyrosine, cysteine, arginine and glutamine in free form and/or salt form (page 3, lines 17-22 and 29-33), and 2) at least one intact protein selected from the group consisting of casein, whey protein, soy protein, collagen or wheat protein (page 3, lines 1-5), wherein said composition provides a ratio of total essential amino acids and, optionally, conditionally essential amino acids to total amino acids ranging from about 0.60 to about 0.90 (page 6, lines 20-27) and wherein said leucine, in free and/or salt form, is present in an amount of at least about 25% by weight based on the weight of intact protein (page 4, lines 1-15); and b) a second composition comprising an anti-cancer drug, wherein said anticancer drug is 5-fluorouracil, mitomycin-C, adriamycin, chloroethyl nitrosureas or methotrexate (page 14, line 29 to page 15, line 2).

Independent Claim 23 is directed to a composition consisting essentially of: leucine (page 3, lines 7-15 and 24-27) and at least one essential amino acid selected from the group consisting of isoleucine, lysine, methionine, phenylalanine, threonine, tryptophan, valine or histidine in free and/or salt form (page 3, lines 17-22 and 29-33), wherein leucine, in free and/or salt form, is present in an amount of at least about 25% by weight based on the weight of total amino acids (page 3, lines 7-15 and 24-27).

Independent Claim 24 is directed to a composition consisting essentially of: leucine (page 3, lines 7-15 and 24-27) and at least one essential amino acid selected from the group consisting of isoleucine, lysine, methionine, phenylalanine, threonine, tryptophan, valine, or histidine in free and/or salt form (page 3, lines 17-22 and 29-33), wherein total leucine is present in an amount of at least about 25% by weight based on the weight of total amino acids (page 3, lines 7-15 and 24-27).

Independent Claim 25 is directed to a composition consisting essentially of: a) leucine (page 3, lines 7-15 and 24-27) and at least one essential amino acid selected from the group consisting of isoleucine, lysine, methionine, phenylalanine, threonine, tryptophan, valine, or histidine (page 3, lines 17-22 and 29-33) and, optionally, at least one conditionally essential

amino acid selected from the group consisting of tyrosine, cysteine, arginine and glutamine in free form and/or salt form (page 3, lines 17-22 and 29-33), wherein said leucine, in free and/or salt form, is present in an amount of at least about 25% (page 3, lines 7-15 and 24-27), and b) at least one intact protein selected from the group consisting of casein, whey protein, soy protein, collagen or wheat protein (page 3, lines 1-5), wherein said composition provides a ratio of total essential amino acids and, optionally, conditionally essential amino acids, to total amino acids ranging from about 0.60 to about 0.90 (page 6, lines 20-27).

Independent Claim 28 is directed to a kit (page 15, line 21-27) comprising: a) a first composition consisting essentially of: 1) leucine (page 3, lines 7-15 and 24-27) and at least one essential amino acid in free form and/or salt form selected from the group consisting of isoleucine, lysine, methionine, phenylalanine, threonine, tryptophan, valine, or histidine (page 3, lines 17-22 and 29-33) and, optionally, at least one conditionally essential amino acid selected from the group consisting of tyrosine, cysteine, arginine and glutamine in free form and/or salt form (page 3, lines 17-22 and 29-33), wherein said leucine, in free and/or salt form, is present in an amount of at least about 25% (page 3, lines 7-15 and 24-27), and 2) at least one intact protein selected from the group consisting of casein, whey protein, soy protein, collagen or wheat protein (page 3, lines 1-5), wherein said composition provides a ratio of total essential amino acids and, optionally, conditionally essential amino acids to total amino acids ranging from about 0.60 to about 0.90 (page 6, lines 20-27); and b) a second composition comprising an anti-cancer drug, wherein said anticancer drug is 5-fluorouracil, mitomycin-C, adriamycin, chloroethyl nitrosureas or methotrexate (page 14, line 29 to page 15, line 2).

Although specification citations are given in accordance with 37 C.F.R. §1.192(c), these reference numerals and citations are merely examples of support in the specification for the terms used in this section of the Brief. There is no intention to suggest in any way that the terms of the claims are limited to the examples in the specification. As demonstrated by the references numerals and citations, the claims are fully supported by the specification as required by law. However, it is improper under the law to read limitations from the specification into the claims. Pointing out specification support for the claim terminology in accordance with Rule 1.192(c) does not in any way limit the scope of the claims to those examples from which they find support. Nor does this exercise provide a mechanism for circumventing the law precluding reading limitations into the claims from the specification. In short, the references numerals and

specification citations are not to be construed as claim limitations or in any way used to limit the scope of the claims.

VI. GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL

1. Claims 3-4, 7-11, 13-14, 16 and 26 stand rejected under 35 U.S.C. §103(a) as being unpatentable over U.S. Patent No. 6,387,883 to Abbruzzese, et al. ("*Abbruzzese*"). A copy of *Abbruzzese* is attached hereto as Exhibit C in the Evidence Appendix.

2. Claims 1-2 and 23-24 stand rejected under 35 U.S.C. §103(a) as being unpatentable over U.S. Patent No. 4,898,879 to Madsen, et al. ("*Madsen*"). A copy of *Madsen* is attached hereto as Exhibit D in the Evidence Appendix.

3. Claims 3-4, 7, 17, 25 and 27-28 stand rejected under 35 U.S.C. §103(a) as being unpatentable over U.S. Patent No. 6,420,342 to Hageman, et al. ("*Hageman*") in view of U.S. Patent No. 6,953,679 to Salvati, et al. ("*Salvati*"). Copies of *Hageman* and *Salvati* are attached hereto as Exhibits E and F, respectively, in the Evidence Appendix.

VII. ARGUMENT

A. LEGAL STANDARDS

Obviousness under 35 U.S.C. §103

The Federal Circuit has held that the legal basis for a determination of obviousness under 35 U.S.C. § 103 is:

> whether the claimed invention as a whole would have been obvious to a person of ordinary skill in the art at the time the invention was made...The foundational facts for the prima facie case of obviousness are: (1) the scope and content of the prior art; (2) the difference between the prior art and the claimed invention; and (3) the level of ordinary skill in the art...Moreover, objective indicia such as commercial success and long felt need are relevant to the determination of obviousness...Thus, each obviousness determination rests on its own facts.

In re Mayne, 41 U.S.P.Q. 2d 1451, 1453 (Fed. Cir. 1997).

In making this determination, the Examiner has the initial burden of proving a *prima facie* case of obviousness. *In re Rijckaert*, 9 F.3d 1531, 1532, 28 U.S.P.Q. 2d 1955, 1956 (Fed. Cir. 1993). This burden may only be overcome "by showing some objective teaching in the prior art or that knowledge generally available to one of ordinary skill in the art would lead that individual to combine the relevant teachings." *In re Fine*, 837 F.2d 1071, 1074, 5 U.S.P.Q. 2d 1596, 1598 (Fed. Cir. 1988). "If the examination at the initial stage does not produce a prima facie case of unpatentability, then without more the applicant is entitled to grant of the patent." *In re Oetiker*, 24 U.S.P.Q. 2d 1443, 1444 (Fed. Cir. 1992).

Moreover, the Examiner must provide explicit reasons why the claimed invention is obvious in view of the prior art. The Supreme Court has emphasized that when formulating a rejection under 35 U.S.C. § 103(a) based upon a combination of prior art elements it remains necessary to identify the reason why a person of ordinary skill in the art would have combined the prior art elements in the manner claimed. *KSR v. Teleflex*, 127 S. Ct. 1727 (2007).

Of course, references must be considered as a whole and those portions teaching against or away from the claimed invention must be considered. *Bausch & Lomb, Inc. v. Barnes-Hind/Hydrocurve Inc.*, 796 F.2d 443 (Fed. Cir. 1986). "A prior art reference may be considered to teach away when a person of ordinary skill, upon reading the reference would be discouraged

from following the path set out in the reference, or would be led in a direction divergent from the path that was taken by the Applicant." *Monarch Knitting Mach. Corp. v. Fukuhara Indus. Trading Co., Ltd.*, 139 F.3d 1009 (Fed. Cir. 1998) (quoting *In re Gurley*, 27 F.3d 551 (Fed. Cir. 1994)).

B. THE CLAIMED INVENTION

There are eight independent claims on appeal: Claims 1-3, 17, 23-25 and 28. Independent Claim 1 is directed to a composition comprising leucine and at least one essential amino acid selected from the group consisting of isoleucine, lysine, methionine, phenylalanine, threonine, tryptophan, valine or histidine in free and/or salt form. The leucine, in free and/or salt form, is present in an amount of at least about 25% to about 95% by weight based on the weight of total amino acids. The composition provides a ratio of total essential amino acids to total amino acids ranging from about 0.60 to about 0.90.

Independent Claim 2 is directed to a composition comprising leucine and at least one essential amino acid selected from the group consisting of isoleucine, lysine, methionine, phenylalanine, threonine, tryptophan, valine, or histidine in free and/or salt form. The total leucine is present in an amount of at least about 25% to about 35% by weight based on the weight of total amino acids. The composition provides a ratio of total essential amino acids to total amino acids ranging from about 0.60 to about 0.90.

Independent Claim 3 is directed to a composition comprising leucine and at least one essential amino acid in free form and/or salt form selected from the group consisting of isoleucine, lysine, methionine, phenylalanine, threonine, tryptophan, valine, or histidine and, optionally, at least one conditionally essential amino acid selected from the group consisting of tyrosine, cysteine, arginine and glutamine in free form and/or salt form. The composition further comprises at least one intact protein selected from the group consisting of casein, whey protein, soy protein, collagen or wheat protein. The composition provides a ratio of total essential amino acids and, optionally, conditionally essential amino acids to total amino acids ranging from about 0.60 to about 0.90. The leucine, in free and/or salt form, is present in an amount of at least about 25% by weight based on the weight of intact protein.

Independent Claim 17 is directed to a kit comprising a first composition comprising: 1) leucine and at least one essential amino acid in free form and/or salt form selected from the group consisting of isoleucine, lysine, methionine, phenylalanine, threonine, tryptophan, valine, or histidine and, optionally, at least one conditionally essential amino acid selected from the group consisting of tyrosine, cysteine, arginine and glutamine in free form and/or salt form, and 2) at least one intact protein selected from the group consisting of casein, whey protein, soy protein, collagen or wheat protein. The composition provides a ratio of total essential amino acids and, optionally, conditionally essential amino acids to total amino acids ranging from about 0.60 to about 0.90. The leucine, in free and/or salt form, is present in an amount of at least about 25% by weight based on the weight of intact protein. The kit further comprises a second composition comprising an anti-cancer drug, wherein said anticancer drug is 5-fluorouracil, mitomycin-C, adriamycin, chloroethyl nitrosureas or methotrexate.

Independent Claim 23 is directed to a composition consisting essentially of leucine and at least one essential amino acid selected from the group consisting of isoleucine, lysine, methionine, phenylalanine, threonine, tryptophan, valine or histidine in free and/or salt form. The leucine, in free and/or salt form, is present in an amount of at least about 25% by weight based on the weight of total amino acids.

Independent Claim 24 is directed to a composition consisting essentially of leucine and at least one essential amino acid selected from the group consisting of isoleucine, lysine, methionine, phenylalanine, threonine, tryptophan, valine, or histidine in free and/or salt form. The total leucine is present in an amount of at least about 25% by weight based on the weight of total amino acids.

Independent Claim 25 is directed to a composition consisting essentially of leucine and at least one essential amino acid selected from the group consisting of isoleucine, lysine, methionine, phenylalanine, threonine, tryptophan, valine, or histidine and, optionally, at least one conditionally essential amino acid selected from the group consisting of tyrosine, cysteine, arginine and glutamine in free form and/or salt form. The leucine, in free and/or salt form, is present in an amount of at least about 25%. The composition further consists essentially of at least one intact protein selected from the group consisting of casein, whey protein, soy protein, collagen or wheat protein. The composition provides a ratio of total essential amino acids

and, optionally, conditionally essential amino acids, to total amino acids ranging from about 0.60 to about 0.90.

Independent Claim 28 is directed to a kit comprising a first composition consisting essentially of leucine and at least one essential amino acid in free form and/or salt form selected from the group consisting of isoleucine, lysine, methionine, phenylalanine, threonine, tryptophan, valine, or histidine and, optionally, at least one conditionally essential amino acid selected from the group consisting of tyrosine, cysteine, arginine and glutamine in free form and/or salt form. The leucine, in free and/or salt form, is present in an amount of at least about 25%. The composition further consists essentially of at least one intact protein selected from the group consisting of casein, whey protein, soy protein, collagen or wheat protein. The composition provides a ratio of total essential amino acids and, optionally, conditionally essential amino acids to total amino acids ranging from about 0.60 to about 0.90. The kit further comprises a second composition comprising an anti-cancer drug, wherein said anticancer drug is 5-fluorouracil, mitomycin-C, adriamycin, chloroethyl nitrosureas or methotrexate.

Appellant has found that when dietary intake is limited below the optimal level for physiological or patho-physiological reasons, a dietary supplement must be more effective than normal food intake in order to provide a benefit. This is because in this circumstance, when a dietary supplement is given, normal food intake is likely to be reduced by a calorically equivalent amount. Consequently, a supplement designed to limit cancer cachexia, for example, should stimulate muscle protein synthesis to a greater extent than normal food intake and should not interfere with the response to meal intake. Trials of conventional nutritional supplements in patients with cancer cachexia have failed to show appreciable benefit in terms of weight gain or quality of life. Accordingly, there is a need for effective nutritional approaches capable of treating, preventing or ameliorating the effects of tumor-induced weight loss due to, for example, cancer cachexia and/or anorexia.

Appellant has surprisingly found that free essential amino acids are a significant factor for amino acid-induced stimulation of muscle protein anabolism. See specification, Example 1. Appellant has also surprisingly found that formulations containing free essential amino acids as compared to a formulation containing intact protein alone is optimal. See specification, Example 2. In addition, Appellant has surprisingly found that nutritional compositions comprising a

mixture of essential amino acids in free form and/or in salt form that have particularly high amounts of leucine (e.g. at least 25% or more) had a stimulatory effect on muscle protein synthesis. See specification, Example 3.

Appellant has further surprisingly and unexpectedly found that particularly useful compositions for promotion of muscle protein synthesis or controlling tumor-induced weight loss, such as cachexia, e.g. cancer cachexia, may be obtained by combining essential amino acids in free form and/or in salt form with intact protein. The effect of such a combination is greater than the effect that can be achieved with either type of combination partner alone.

C. THE REJECTION OF CLAIMS 3-4, 7-11, 13-14, 16 AND 26 UNDER 35 U.S.C. §103(A) TO *ABBRUZZESE* SHOULD BE REVERSED BECAUSE THE EXAMINER HAS FAILED TO ESTABLISH A *PRIMA FACIE* CASE OF OBVIOUSNESS WITH RESPECT TO CLAIMS 3-4, 7-11, 13-14, 16 AND 26

1. *Abbruzzese* fails to disclose or suggest every element of the claimed invention

Independent Claim 3 recites, in part, leucine, in free and/or salt form, present in an amount of at least about 25% by weight based on the weight of intact protein. Independent Claim 3 also recites, in part, a ratio of total essential amino acids and, optionally, conditionally essential amino acids to total amino acids ranging from about 0.60 to about 0.90. Appellant has surprisingly found through experimentation that nutritional compositions comprising a mixture of essential amino acids in free form and/or in salt form that have particularly high amounts of leucine (e.g. at least 25% or more) had a stimulatory effect on muscle protein synthesis. See specification, Example 3. In contrast, Appellant respectfully submits that *Abbruzzese* fails to disclose or suggest every element of independent Claim 3.

Abbruzzese fails to disclose or suggest that leucine, in free and/or salt form, is present in an amount of at least about 25% by weight based on the weight of intact protein as required by independent Claim 3. *Abbruzzese* also fails to disclose or suggest a ratio of total essential amino acids and, optionally, conditionally essential amino acids to total amino acids ranging from about 0.60 to about 0.90 as required by independent Claim 3. The Patent Office admits same. See final Office Action, page 5.

For at least the reasons discussed above *Abbruzzese* fail to disclose or suggest every element of independent Claim 3. Accordingly, Appellant respectfully submits that Claim 3, along with Claims 4, 7-11, 13-14, 16 and 26 that depend from Claim 3, are novel, nonobvious and distinguishable from the cited reference and are in condition for allowance.

2. The skilled artisan would have no reason to arrive at the claimed invention in view of *Abbruzzese*

Appellant respectfully submits that the skilled artisan would not arrive at the claimed invention using *Abbruzzese* in the absence of hindsight because the cited reference fails to recognize the surprising and unexpected benefits of the claimed compositions having optimal amounts of leucine and essential amino acids. Appellant respectfully submits that the Examiner is using Appellant's patent application as a road map for creating hindsight obviousness and has failed to set forth sufficient reasons for how the skilled artisan would arrive at the claimed invention in view of *Abbruzzese*.

Abbruzzese is directed to methods and nutritional compositions for preventing and treating cachexia and anorexia. *Abbruzzese's* composition includes effective amounts of (1) ω3 fatty acids, such as α-linolenic acid, stearidonic acid, eicosapentaenoic acid, docosapentaenoic acid, docosahexaenoic acid or mixtures thereof; (2) branched-chain amino acids, such as valine, leucine, isoleucine or mixtures thereof; with or without reduced levels of tryptophan and 5-hydroxytryptophan; and (3) an anti-oxidant system selected from the group consisting of beta-carotene, vitamin C, vitamin E, selenium, or mixtures thereof. See *Abbruzzese*, column 3, lines 15-56.

In the only example that utilizes leucine, *Abbruzzese* teaches an amino acid profile for his nutritional composition with leucine in an amount of 9.08 g/100 g protein (i.e. 9.08%), which is substantially lower than that of the present claims and actually teaches away from same. See *Abbruzzese*, column 9, line 17. Moreover, in *Abbruzzese's* composition, the ratio of total essential amino acids and conditionally essential amino acids to total amino acids is 0.51, which is also much lower than that of the present claims. As a result, there is no teaching or suggestion to the skilled artisan to optimize the leucine range and amino acid ratios of *Abbruzzese* in accordance with that of the present claims in the absence of hindsight.

The Examiner asserts that finding the optimal ranges of leucine or ratio of total essential amino acids and conditionally essential amino acids to total amino acids would have been obvious to the skilled artisan for the sole reason that *Abbruzzese* teaches a nutritional composition for treating cancer cachexia. However, this conclusory statement is not sufficient to establish a *prima facie* case of obviousness without some objective reason to utilize the teachings of the references to arrive at the invention. *Ex parte Levengood*, 28 USPQ2d 1300 (Bd. Pat. App. & Inter. 1993). There must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness by the Examiner. *In re Kahn*, 441 F.3d 977, 988, 78 USPQ2d 1329, 1336 (Fed. Cir. 2006).

Appellant respectfully submits that there is absolutely no guidance in *Abbruzzese* for one of skill in the art to choose the active components and effective amount of the components present in the instant claims to achieve the unexpectedly improved composition as Appellant has done. To arrive at the claimed optimal ranges of leucine or ratio of total essential amino acids and conditionally essential amino acids to total amino acids in accordance with Claim 3, the skilled artisan would have to select these specific components from the teachings of the numerous ω3 fatty acids, branched-chain amino acids, carbohydrates, and anti-oxidant systems taught by *Abbruzzese* and then combine them in the specified amounts in a composition. To accomplish this, the skilled artisan would have to perform an undue amount of experimentation to arrive at the specific components and ranges recited by Claim 3. The sheer quantity of experimentation necessary to arrive at the composition would be excessive. Moreover, *Abbruzzese* does not provide any direction or guidance for using leucine over any other amino acid, and there would be thousands of combinations that would not include any of leucine.

In sum, the skilled artisan would have no reason to arrive at the optimal conditions of the claimed invention using *Abbruzzese* in the absence of hindsight. Moreover, *Abbruzzese* fails to even recognize the advantages, benefits and/or properties of compositions having leucine and essential amino acids in accordance with the present claims. Instead, Appellant respectfully submits that the Examiner is improperly using Appellant's patent application as a road map for creating hindsight obviousness. Accordingly, Appellant respectfully submits that Claim 3, along with Claims 4, 7-11, 13-14, 16 and 26 that depend from Claim 3, are novel, nonobvious and distinguishable from the cited reference and are in condition for allowance.

D. THE REJECTION OF CLAIMS 1-2 AND 23-24 UNDER 35 U.S.C. §103(A) TO *MADSEN* SHOULD BE REVERSED BECAUSE THE EXAMINER HAS FAILED TO ESTABLISH A *PRIMA FACIE* CASE OF OBVIOUSNESS WITH RESPECT TO CLAIMS 1-2 AND 23-24

1. *Madsen* fails to disclose or suggest every element of the claimed invention

Independent Claims 1-2 recite, in part, leucine, in free and/or salt form, present in an amount of at least about 25% to about 95% by weight based on the weight of total amino acids. Independent Claims 23-24 recite, in part, leucine, in free and/or salt form, present in an amount of at least about 25% by weight based on the weight of total amino acids. Appellant has surprisingly found through experimentation that nutritional compositions comprising a mixture of essential amino acids in free form and/or in salt form that have particularly high amounts of leucine (e.g. at least 25% or more) had a stimulatory effect on muscle protein synthesis. See specification, Example 3. In contrast, Appellant respectfully submits that *Madsen* fails to disclose or suggest every element of independent Claims 1-2 and 23-24.

Madsen fails to disclose or suggest that leucine, in free and/or salt form, is present in an amount of at least about 25% to about 95% by weight based on the weight of total amino acids as required by independent Claims 1-2. *Madsen* also fails to disclose or suggest that leucine, in free and/or salt form, is present in an amount of at least about 25% by weight based on the weight of total amino acids as required by independent Claims 23-24. The Patent Office admits same. See final Office Action, page 9.

For at least the reasons discussed above, *Madsen* fails to disclose or suggest every element of independent Claims 1-2 and 23-24. Accordingly, Appellant respectfully submits that Claims 1-2 and 23-24 are novel, nonobvious and distinguishable from the cited reference and are in condition for allowance.

2. The skilled artisan would have no reason to arrive at the claimed invention in view of *Madsen*

Appellant respectfully submits that the skilled artisan would not arrive at the claimed invention using *Madsen* in the absence of hindsight because the cited reference is entirely directed to compositions utilizing different nutritional ingredients for different intended purposes. Moreover, *Madsen* fails to even recognize the surprising and unexpected benefits of the claimed compositions having optimal amounts of leucine and essential amino acids. Appellant respectfully submits that the Examiner is using Appellant's patent application as a road map for creating hindsight obviousness and has failed to set forth sufficient reasons for how the skilled artisan would arrive at the claimed invention in view of *Madsen*.

Madsen is directed to compositions and methods for nutritional management of hepatic (liver) failure. *Madsen* discloses amino acid compositions designed to meet the altered metabolic needs of patients suffering from hepatic failure and the attendant derangements of normal amino acid metabolism characterized by this clinical condition. *Madsen* discloses that its nutritional composition can comprise "about 19.4 to 19.8% of leucine." Accordingly, *Madsen's* leucine level is lower than that of the claimed compositions, which teaches away from Claims 1-2 and 23-24.

The Examiner asserts that finding the optimal ranges of leucine would have been obvious to the skilled artisan for the sole reason that *Madsen* teaches a nutritional composition for treating different disorders. However, this conclusory statement is not sufficient to establish a *prima facie* case of obviousness without some objective reason to utilize the teachings of the references to arrive at the invention. *Ex parte Levengood*, 28 USPQ2d 1300 (Bd. Pat. App. & Inter. 1993). There must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness by the Examiner. *In re Kahn*, 441 F.3d 977, 988, 78 USPQ2d 1329, 1336 (Fed. Cir. 2006).

Appellant respectfully submits that there is absolutely no guidance in *Madsen* for one of skill in the art to choose the effective range of leucine recited by Claims 1-2 and 23-24 to achieve the unexpectedly improved composition as Appellant has done. Leucine is one of many listed amino acids and *Madsen* fails to recognize or suggest any superior benefit from increased levels of leucine beyond what is taught. Consequently, the skilled artisan would have no reason to

optimize the leucine range of *Madsen* in accordance with that of the present claims in the absence of hindsight.

In sum, the skilled artisan would have no reason to arrive at the optimal conditions of the claimed invention using *Madsen* in the absence of hindsight. Moreover, *Madsen* fails to even recognize the advantages, benefits and/or properties of compositions having leucine in accordance with the present claims. Instead, Appellant respectfully submits that the Examiner is improperly using Appellant's patent application as a road map for creating hindsight obviousness. Accordingly, Appellant respectfully submits that Claims 1-2 and 23-24 are novel, nonobvious and distinguishable from the cited reference and are in condition for allowance.

E. THE REJECTION OF CLAIMS 3-4, 7, 17, 25 AND 27-28 UNDER 35 U.S.C. §103(A) TO *HAGEMAN* AND *SALVATI* SHOULD BE REVERSED BECAUSE THE EXAMINER HAS FAILED TO ESTABLISH A *PRIMA FACIE* CASE OF OBVIOUSNESS WITH RESPECT TO CLAIMS 3-4, 7, 17, 25 AND 27-28

1. *Hageman* and *Salvati* alone or in combination fail to disclose or suggest every element of the claimed invention

Independent Claims 3, 17, 25 and 28 recite, in part, leucine, in free and/or salt form, present in an amount of at least about 25% by weight based on the weight of intact protein. Independent Claims 3, 17, 25 and 28 also recite, in part, a ratio of total essential amino acids and, optionally, conditionally essential amino acids to total amino acids ranging from about 0.60 to about 0.90. In addition, independent Claims 25 and 28 recite, in part, a composition consisting essentially of a) leucine and at least one essential amino acid selected from the group consisting of isoleucine, lysine, methionine, phenylalanine, threonine, tryptophan, valine, or histidine, and b) at least one intact protein selected from the group consisting of casein, whey protein, soy protein, collagen or wheat protein. In contrast, Appellant respectfully submits that *Hageman* and *Salvati* alone or in combination fail to disclose or suggest every element of independent Claims 3, 17, 25 and 28.

Hageman and *Salvati* fail to disclose or suggest leucine, in free and/or salt form, present in an amount of at least about 25% by weight based on the weight of intact protein as required by independent Claims 3, 17, 25 and 28. *Hageman* and *Salvati* also fail to disclose or suggest a

ratio of total essential amino acids and, optionally, conditionally essential amino acids to total amino acids ranging from about 0.60 to about 0.90 as required by independent Claims 3, 17, 25 and 28. Finally, *Hageman* and *Salvati* fail to disclose or suggest a composition consisting essentially of a) leucine and at least one essential amino acid selected from the group consisting of isoleucine, lysine, methionine, phenylalanine, threonine, tryptophan, valine, or histidine, and b) at least one intact protein selected from the group consisting of casein, whey protein, soy protein, collagen or wheat protein as required by Claims 25 and 28. In contrast, *Hageman* discloses a nutritional, pharmaceutical or dietetic preparation that requires ribose and folic acid. *Salvati* discloses fused cyclic compounds and methods of using such compounds in the treatment of nuclear hormone receptor-associated diseases such as cancer and immune disorders.

For at least the reasons discussed above, *Hageman* and *Salvati* alone or in combination fail to disclose or suggest every element of independent Claims 3, 17, 25 and 28. Accordingly, Appellant respectfully submits that Claims 3, 17, 25 and 28, along with Claims 4, 7 and 27 that depend from Claim 3, are novel, nonobvious and distinguishable from the cited references and are in condition for allowance.

2. The skilled artisan would have no reason to combine *Hageman* and *Salvati* to arrive at the claimed invention

Appellant respectfully submits that the skilled artisan would not arrive at the claimed invention using *Hageman* and *Salvati* in the absence of hindsight because the cited references are entirely directed to compositions utilizing different nutritional ingredients for different intended purposes. Moreover, *Hageman* and *Salvati* fail to even recognize the surprising and unexpected benefits of the claimed compositions having optimal amounts of leucine and essential amino acids. Appellant respectfully submits that the Examiner is using Appellant's patent application as a road map for creating hindsight obviousness and has failed to set forth sufficient reasons for how the skilled artisan would arrive at the claimed invention in view of *Hageman* and *Salvati*.

Hageman generally describes a nutritional, pharmaceutical or dietetic preparation that includes effective amounts of ribose and folic acid, optionally combined with other components, such as niacin, histidine, glutamine, orotate, vitamin B6 and other

components. See *Hageman*, column 5, lines 8-52. *Hageman* also discloses products having the following mixture of amino acids as beneficial for muscle growth when consumed in an amount of more than 2 and preferably more than 4 g per daily dose: 3-10 wt % histidine, 5-15 wt % isoleucine, 10-23 wt % leucine, 10-23 wt % lysine, 515 wt % methionine, 5-15 wt % phenylalanine, 5-15 wt % threonine. See *Hageman*, column 6, line 62-column 7, line 1. The maximum level of leucine of *Hageman's* composition is 23%, which is lower than that of the present claims.

Salvati generally describes fused cyclic compounds and methods of using such compounds in the treatment of nuclear hormone receptor-associated diseases such as cancer and immune disorders and pharmaceutical compositions containing such compounds. See *Salvati*, Abstract. *Salvati*, along with *Hageman*, lists leucine as one of many amino acids and fails to recognize or suggest any superior benefit from increased levels of leucine beyond what is taught. Consequently, the skilled artisan would have no reason to optimize the leucine range of *Hageman* and *Salvati* in accordance with that of the present claims in the absence of hindsight.

The Examiner asserts that finding the optimal ranges of leucine or ratio of total essential amino acids and conditionally essential amino acids to total amino acids would have been obvious to the skilled artisan in view of *Hageman* and *Salvati* teachings. However, this conclusory statement is not sufficient to establish a *prima facie* case of obviousness without some objective reason to utilize the teachings of the references to arrive at the invention. *Ex parte Levengood*, 28 USPQ2d 1300 (Bd. Pat. App. & Inter. 1993). There must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness by the Examiner. *In re Kahn*, 441 F.3d 977, 988, 78 USPQ2d 1329, 1336 (Fed. Cir. 2006).

Appellant respectfully submits that there is absolutely no guidance in *Hageman* and *Salvati* for one of skill in the art to choose the active components and effective amount of the components present in the instant claims to achieve the unexpectedly improved composition as Appellant has done. To arrive at the claimed optimal ranges of leucine or ratio of total essential amino acids and conditionally essential amino acids to total amino acids in accordance with Claims 3, 17, 25 and 28, the skilled artisan would have to select these specific components from the numerous components taught by *Hageman* and *Salvati*. *Hageman* teaches the use of ribose, folate, magnesium, niacin, selenium, thiamine, glucose, citrate, histidine, phosphate, sulfate and

vitamin B12 and numerous amino acids as active components in his composition. See *Hageman*, columns 5-6. *Salvati* teaches thousands of possible fused cyclic compounds that can be part of his nutritional composition along with whey protein or casin, amino acids, triglycerides, vitamins, minerals, carnitine, lipoic acid, creatine, and coenzyme Q-10. See *Salvati*, columns 3-8.

The skilled artisan would have to perform an undue amount of experimentation based on the thousands of individual compounds listed by *Hageman* and *Salvati* to arrive at the specific components and ranges recited by Claims 3, 17, 25 and 28. The sheer quantity of experimentation necessary to arrive at the composition would be excessive. Moreover, *Hageman* and *Salvati* do not provide any direction or guidance for using leucine over any other amino acid, and there would be thousands of combinations that would not include any of leucine. As a result, there is no reason that the skilled artisan would optimize the leucine range or amino acid ratios of *Hageman* and *Salvati* in accordance with that of the present claims.

In sum, the skilled artisan would have no reason to arrive at the optimal conditions of the claimed invention using *Hageman* and *Salvati* in the absence of hindsight. *Hageman* and *Salvati* also fail to even recognize the advantages, benefits and/or properties of compositions having leucine and essential amino acids in accordance with the present claims. Instead, Appellant respectfully submits that the Examiner is improperly using Appellant's patent application as a road map for creating hindsight obviousness. Accordingly, Appellant respectfully submits that Claims 3, 17, 25 and 28, along with Claims 4, 7 and 27 that depend from Claim 3, are novel, nonobvious and distinguishable from the cited references and are in condition for allowance.

VIII. CONCLUSION

Appellant respectfully submits that the Examiner has failed to establish a *prima facie* case of obviousness under 35 U.S.C. §103 with respect to the rejections of Claims 1-4, 7-11, 13-14, 16-17 and 23-28. Accordingly, Appellant respectfully submits that the obviousness rejections are erroneous in law and in fact and should therefore be reversed by this Board.

A check in the amount of $510 is submitted herewith to cover the cost of the Appeal Brief. The Director is authorized to charge any additional fees that may be required, or to credit any overpayment to Deposit Account No. 50-4498 in the name of Nestle Nutrition.

Respectfully submitted,

BY _____

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Dated: April 9, 2009

CLAIMS APPENDIX

PENDING CLAIMS ON APPEAL OF U.S. PATENT APPLICATION SERIAL NO. 10/662,678

1. A composition comprising: leucine and at least one essential amino acid selected from the group consisting of isoleucine, lysine, methionine, phenylalanine, threonine, tryptophan, valine or histidine in free and/or salt form, wherein said leucine, in free and/or salt form, is present in an amount of at least about 25% to about 95% by weight based on the weight of total amino acids and wherein said composition provides a ratio of total essential amino acids to total amino acids ranging from about 0.60 to about 0.90.

2. A composition comprising: leucine and at least one essential amino acid selected from the group consisting of isoleucine, lysine, methionine, phenylalanine, threonine, tryptophan, valine, or histidine in free and/or salt form, wherein total leucine is present in an amount of at least about 25% to about 35% by weight based on the weight of total amino acids and wherein said composition provides a ratio of total essential amino acids to total amino acids ranging from about 0.60 to about 0.90.

3. A composition comprising:

a) leucine and at least one essential amino acid in free form and/or salt form selected from the group consisting of isoleucine, lysine, methionine, phenylalanine, threonine, tryptophan, valine, or histidine and, optionally, at least one conditionally essential amino acid selected from the group consisting of tyrosine, cysteine, arginine and glutamine in free form and/or salt form, and

b) at least one intact protein selected from the group consisting of casein, whey protein, soy protein, collagen or wheat protein, wherein said composition provides a ratio of total essential amino acids and, optionally, conditionally essential amino acids to total amino acids ranging from about 0.60 to about 0.90 and wherein said leucine, in free and/or salt form, is present in an amount of at least about 25% by weight based on the weight of intact protein.

4. The composition of claim 3, wherein the essential amino acid comprises leucine and at least one of isoleucine, lysine, methionine, phenylalanine, threonine, tryptophan, valine, or histidine.

7. The composition of claim 3, further comprising methionine in free and/or salt form in an amount of at least about 0.5% to about 5% by weight based on the weight of total amino acids.

8. The composition of claim 3, further comprising an n-3 polyunsaturated fatty acid.

9. The composition of claim 8, wherein the n-3 polyunsaturated fatty acid is chosen from u-linolenic acid, eicosapentaenoic acid and docosahexaenoic acid.

10. The composition of claim 3, further comprising at least about 1 g of eicosapentaenoic acid per serving or at least about 2 g of eicosapentaenoic acid per daily dose.

11. The composition of claim 3, further comprising tocopherol.

13. The composition of claim 11, wherein the tocopherol is present in an amount about 50 mg per serving or at least 150 mg per daily dose.

14. The composition of claim 3, comprising from about 15 g to about 55 g amino acids in free and/or salt form per daily dose.

16. The composition of claim 3, comprising from about 36 g to about 72 g total essential and/or conditionally essential amino acids per serving.

17. A kit comprising:

a) a first composition comprising:

1) leucine and at least one essential amino acid in free form and/or salt form selected from the group consisting of isoleucine, lysine, methionine, phenylalanine, threonine, tryptophan, valine, or histidine and, optionally, at least one conditionally essential amino acid selected from the group consisting of tyrosine, cysteine, arginine and glutamine in free form and/or salt form, and

2) at least one intact protein selected from the group consisting of casein, whey protein, soy protein, collagen or wheat protein, wherein said composition provides a ratio of total essential amino acids and, optionally, conditionally essential amino acids to total amino acids ranging from about 0.60 to about 0.90 and wherein said leucine, in free and/or salt form, is present in an amount of at least about 25% by weight based on the weight of intact protein; and

b) a second composition comprising an anti-cancer drug, wherein said anticancer drug is 5-fluorouracil, mitomycin-C, adriamycin, chloroethyl nitrosureas or methotrexate.

23. A composition consisting essentially of: leucine and at least one essential amino acid selected from the group consisting of isoleucine, lysine, methionine, phenylalanine, threonine, tryptophan, valine or histidine in free and/or salt form, wherein leucine, in free and/or salt form, is present in an amount of at least about 25% by weight based on the weight of total amino acids.

24. A composition consisting essentially of: leucine and at least one essential amino acid selected from the group consisting of isoleucine, lysine, methionine, phenylalanine, threonine, tryptophan, valine, or histidine in free and/or salt form, wherein total leucine is present in an amount of at least about 25% by weight based on the weight of total amino acids.

25. A composition consisting essentially of:

a) leucine and at least one essential amino acid selected from the group consisting of isoleucine, lysine, methionine, phenylalanine, threonine, tryptophan, valine, or histidine and, optionally, at least one conditionally essential amino acid selected from the group consisting of tyrosine, cysteine, arginine and glutamine in free form and/or salt form, wherein said leucine, in free and/or salt form, is present in an amount of at least about 25%, and

b) at least one intact protein selected from the group consisting of casein, whey protein, soy protein, collagen or wheat protein, wherein said composition provides a ratio of total essential amino acids and, optionally, conditionally essential amino acids, to total amino acids ranging from about 0.60 to about 0.90.

26. The composition of claim 3, comprising from about 12 g to about 15 g leucine in free and/or salt form per daily dose.

27. The composition of claim 3, further comprising methionine in free and/or salt form in an amount of at least about 5% to about 7% by weight based on the weight of total amino, acids.

28. A kit comprising:

a) a first composition consisting essentially of:

1) leucine and at least one essential amino acid in free form and/or salt form selected from the group consisting of isoleucine, lysine, methionine, phenylalanine, threonine, tryptophan, valine, or histidine and, optionally, at least one conditionally essential amino acid selected from the group consisting of tyrosine, cysteine, arginine and glutamine in free form and/or salt form, wherein said leucine, in free and/or salt form, is present in an amount of at least about 25%, and

2) at least one intact protein selected from the group consisting of casein, whey protein, soy protein, collagen or wheat protein, wherein said composition provides a ratio of total essential amino acids and, optionally, conditionally essential amino acids to total amino acids ranging from about 0.60 to about 0.90; and

b) a second composition comprising an anti-cancer drug, wherein said anticancer drug is 5-fluorouracil, mitomycin-C, adriamycin, chloroethyl nitrosureas or methotrexate.

EVIDENCE APPENDIX

EXHIBIT A: Final Office Action dated December 15, 2008

EXHIBIT B: Advisory Action mailed on February 24, 2009

EXHIBIT C: U.S. Patent No. 6,387,883 to Abbruzzese, et al. ("*Abbruzzese*"), cited by the Examiner in the Office Action dated December 15, 2008

EXHIBIT D: U.S. Patent No. 4,898,879 to Madsen, et al. ("*Madsen*"), cited by the Examiner in the Office Action dated December 15, 2008

EXHIBIT E: U.S. Patent No. 6,420,342 to Hageman, et al. ("*Hageman*"), cited by the Examiner in the Office Action dated December 15, 2008

EXHIBIT F: U.S. Patent No. 6,953,679 to Salvati, et al. ("*Salvati*"), cited by the Examiner in the Office Action dated December 15, 2008

RELATED PROCEEDINGS APPENDIX

None